UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,385	04/25/2002	Silvia Buervenich	1103326-0677	1420

7470 7590 05/16/2007

WHITE & CASE LLP
PATENT DEPARTMENT
1155 AVENUE OF THE AMERICAS
NEW YORK, NY 10036

EXAMINER	
QIAN, CELINE X	

ART UNIT	PAPER NUMBER
1636	

MAIL DATE	DELIVERY MODE
05/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/019,385	BUERVENICH ET AL.	
	Examiner	Art Unit	
	Celine X. Qian Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20 and 24-37* is/are pending in the application.

4a) Of the above claim(s) *12-20,24-31 and 35-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 March 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *0202*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-20, 24-37 are pending in the application.

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on 2/14/07 is acknowledged. The traversal is on the ground(s) that the amended claim 1 is drawn to an isolated Nurr1 gene, or a functional fragment or variant that comprises the recited mutation, such that the special technical feature would constitutes a contribution over the cited prior art Castillo et al because this reference does not recite these mutations.

This argument is found persuasive. The restriction requirement is re-written and the reasoning for the requirement is discussed below.

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.
In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-11, 32-34, drawn to an isolated Nurrl gene including one or more mutation or a fragment thereof, vector and host cell comprises said gene or fragment.

Group II, claim(s) 12-15, drawn to a protein or a peptide encoded by a gene or fragment of Nurrl.

Group III, claims 16 and 17, drawn to a method of screening for pharmaceutical substance by using a nucleic acid or a peptide of Nurrl mutant or fragment thereof, and a pharmaceutical substance identified.

Group IV, claims 18 and 25, drawn to an antibody raised against a protein encoded by a mutant Nurrl gene, and a pharmaceutical composition comprising said antibody.

Group V, claims 19 and 20, drawn to a transgenic non-human animal comprising a mutant Nurrl gene or fragment.

Group VI, claims 24 and 36, drawn to a method of treating a psychotic condition by administering to a host an effective amount of pharmaceutical composition that is screened by Nurrl nucleic acid or peptide.

Group VII, claims 26 and 27, drawn to a method of detecting the presence of a mutation in exon 3 or Nurrl gene in a biological sample.

Group VIII, claim 28, drawn to a kit comprising reagents for amplification, enzymes for cleavage.

Group IX, claims 29-31, drawn to a method of treating or preventing schizophrenia by correct a mutation in exon 3 or the Nurrl gene.

Group X, claims 35 and 37, drawn to a method for the treatment of a psychotic condition by administering to the patient an antibody raise against protein encoded by mutant Nurrl gene or fragment thereof.

The special technical feature of each group is listed as following. The special technical feature of group I an isolated Nurr1 gene, or a functional fragment or variant that has a recited mutation as in claim 1; the special technical feature of group II is a protein or peptide that encoded by the mutated Nurr1 gene; the special technical feature of group III is a method of screening for pharmaceutically active substances with either the nucleic acid or peptide of Nurr1 mutant; the special technical feature of group IV is an antibody raised against a protein encoded by a mutant Nurr1 gene; the special technical feature of group V is a non-human animal comprising a mutant Nurr1 gene; the special technical feature of group VI is treating psychotic condition by a pharmaceutical compound; the special technical feature of group VII is detecting mutation from biological sample; the special technical feature of group VIII is reagents, enzymes for specific cleavage and labels; the special technical feature of group IX is correction of mutation in exon 3 or Nurr1 gene; the special technical feature of group X is treating psychotic condition with an antibody. Since the invention of each group has a unique special technical feature that is different from each other, the unity of invention does not exist.

The requirement is still deemed proper and is therefore made FINAL.

Applicants further argue that the recited mutation all occurs in exon 3 of Nurr1 gene and has a common link between the Nurr1 gene and neuropsychiatric disorders. Applicants assert

that all the mutations lead to impaired Nurr1 transcriptional activity, thus each recited mutation has common property. Applicants further argue that the statement of "each molecule of a mutant Nurr1 gene or protein is chemically and structurally distinct from each other thus do not share a common special technical feature" is mistaken by analogy to chemical compounds that are considered a genus. Applicants thus conclude that the all the mutation should be examined together.

In response to Applicant's argument, Applicant's attention is directed to MPEP 1850 "When the Markush grouping is for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled:

(A) All alternatives have a common property or activity; and

(B)(1) A common structure is present, i.e., a significant structural element is shared by all of the alternatives; or

(B)(2) In cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.

In paragraph (B)(1), above, the words "significant structural element is shared by all of the alternatives" refer to cases where the compounds share a common chemical structure which occupies a large portion of their structures, or in case the compounds have in common only a small portion of their structures, the commonly shared structure constitutes a structurally distinctive portion in view of existing prior art, and the common structure is essential to the common property or activity. The structural element may be a single component or a combination of individual components linked together. In paragraph (B)(2), above, the words

"recognized class of chemical compounds" mean that there is an expectation from the knowledge in the art that members of the class will behave in the same way in the context of the claimed invention. In other words, each member could be substituted one for the other, with the expectation that the same intended result would be achieved."

According to the cited section of MPEP, the situation described in (B)(2) applies to the instant situation because Applicants state that each mutation has the same function which lead to impaired transcriptional activity. The lack of unity requirement between each mutation is withdrawn based on Applicant's admission that each mutation or combination of mutation has same function, and could be substitute one for other. Therefore, all recited mutation will be examined together.

Accordingly, claims 12-20, 24-31 and 35-37 are withdrawn from consideration for being directed to non-elected subject matter. Claims 1-11 and 32-34 are currently under examination.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 9 and 33 are rejected under 35 USC §101 because the claimed invention is directed to non-statutory subject matter. The term "cell" as defined by the specification at page 18, 1st full paragraph states that the cell is present or intended to be present in a human being,

said cell becoming integrated into the human being and therefore being an inseparable part of the human itself. The scope of the claim, therefore, encompasses a human being, which is non-statutory subject matter. As such, the recitation of the limitation "an isolated" would be remedial. See 1077 O.G. 24, April 21, 1987.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11, 32-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description requirement is set forth by 35 U.S.C. 112, first paragraph which states that the: "*specification* shall contain a written description of the invention . . .[emphasis added]." The written description requirement has been well established and characterized in the case law. A specification must convey to one of skill in the art that "as of the filing date sought, [the inventor] was in possession of the invention." See *Vas Cath v. Mahurkar* 935 F.2d 1555, 1560 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Applicant may show that he is in "possession" of the invention claimed by describing the invention with all of its claimed limitations "by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the

claimed invention." See *Lockwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

In analyzing whether the written description requirement is met, it is first determined whether a representative number of species have been described by their complete structure. Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics. Claim 1 recites an isolated Nurr1 gene which comprises one or more of the recited mutations, and functional fragments or variants that also include said mutations. The claimed genus of gene, fragments and variants includes potentially a large number of nucleic acid sequences of various length and structure/sequences as long as it has a substitution of Met to Val, His to Arg, or a deletion of a Tyr. The specification discloses that three specific mutations in exon 3 (not include Y121del) of human Nurr1 gene, Met97Val, His103Arg, and Y122del, which results in the reduction in transcription activation of said gene, and is linked to schizophrenia and bipolar disorder. However, it does not teach whether mutation at the same position in Nurr1 from other species, for example, rat, would result in the same loss of function (in fact, it is unclear whether the amino acid at 97, 103 and 122 is conserved in other species). Further, the specification fails to teach any functional fragments that comprises said mutation would still encodes a Nurr1 protein that has same activation potential as the full length gene. Moreover, the specification fails to teach any variants, which would includes proteins have totally unrelated sequences, which still has the claimed function. Lastly, regarding claim 7, the instant specification does not disclose any nucleic acid capable of hybridizing to a variant, a functional fragment or the Nurr1 gene which still possess the claimed function. In view of the broad genus of nucleic acid claimed, the specification fails to describe a

representative species of their complete structure and other identifying characteristics. Therefore, the written description requirement is not met.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11, 32-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 1, 4-6, 10, the recitation of "an isolated Nurr1, or a functional fragment or variant thereof...includes one or more mutations selected from the group consisting of Met97Val..." renders the claim indefinite because a nucleic acid cannot have a mutation of Met to Val. Met and Val are amino acid sequence, not nucleic acid sequence. As such, the metes and bounds of the claim cannot be established. Claims 2, 3, 7-9, 11, 32-34 are rejected for same reason because they depend on the above claims.

Regarding claim 2, the recitation of "the exons" renders the claim indefinite because it is unclear which exon applicant is referring to. Since claim 1 is directed to an isolated Nurr1 gene or fragments, it is unclear whether the fragment claimed in claim 2 includes all exons of Nurr1 or only a few of them.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 7 is rejected under 35 U.S.C. 102(b) as being anticipated by Odila Saucede-Cardenas et al (see IDS).

The sequence disclose on page 4014 2nd col., first line as the 5' primer located in exon 3 is able to hybridize specifically to the claimed gene or fragments. Therefore, this reference discloses the instantly claimed invention.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joe Woitach Ph.D. can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Celine X Qian Ph.D.
Examiner
Art Unit 1636

CELINE QIAN, PH.D.
PRIMARY EXAMINER